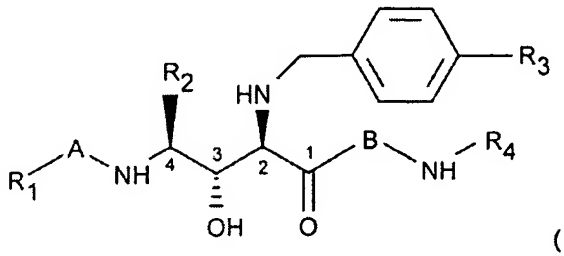
Amendments to the Claims

This Listing of the Claims will replace all prior versions, and listings, of claims in the application.

Listing of the Claims:

1. (Withdrawn) Use of a 2,4-diamino-3-hydroxycarboxylic acid of formula I



(I)

wherein

A and B independently represent a bond or an unsubstituted or substituted amino acyl moiety;

R_1 represents hydrogen; an amino protecting group; or a group of formula R_5Y- wherein

R_5 represents hydrogen or an unsubstituted or substituted alkyl, alkenyl, alkinyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, heterocyclyl or heterocyclylalkyl group; and

Y represents -CO-; -NH-CO-; -NH-CS-; $-SO_2-$; -O-CO-; or -O-CS-;

R_2 represents the side chain of a natural amino acid; an alkyl, arylalkyl, heteroarylalkyl or cycloalkylalkyl group; or trimethylsilylmethyl, 2-thienylmethyl or styrylmethyl;

R_3 represents halogen, alkyl, alkoxy or hydroxyalkoxy; and

R_4 represents 2(R)-hydroxyindan-1(S)-yl; (S)-2-hydroxy-1-phenylethyl; or 2-hydroxy-benzyl unsubstituted or substituted in 4-position by methoxy;

in free form or in pharmaceutically acceptable salt or complex form in the manufacture of a pharmaceutical composition for the treatment of a proliferative disease responsive to an inhibition of the multicatalytic proteasome complex.

2. (Withdrawn) Use of a 2,4-diamino-3-hydroxycarboxylic acid of formula I according to claim 1, wherein A and B independently represent a bond or an amino acyl moiety, which is unsubstituted or substituted by alkyl or alkoxycarbonylalkyl;

R_1 represents hydrogen; an amino protecting group; or a group of formula R_5Y- wherein

R_5 represents hydrogen or an unsubstituted or substituted alkyl, alkenyl, alkinyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, heterocyclyl or heterocyclylalkyl group; and

Y represents -CO-; -NH-CO-; -NH-CS-; -SO_2-; -O-CO-; or -O-CS-;

R_2 represents the side chain of a natural amino acid; an alkyl, arylalkyl, heteroarylalkyl or cycloalkylalkyl group; or trimethylsilylmethyl, 2-thienylmethyl or styrylmethyl;

R_3 represents halogen, alkyl, alkoxy or hydroxyalkoxy; and

R_4 represents 2(R)-hydroxyindan-1(S)-yl; (S)-2-hydroxy-1-phenylethyl; or 2-hydroxy-benzyl unsubstituted or substituted in 4 position by methoxy.

3. (Withdrawn) Use of a 2,4-diamino-3-hydroxycarboxylic acid of formula I according to claim 1, wherein

A and B independently represent a bond or an amino acyl moiety, which is unsubstituted or substituted by alkyl or alkoxycarbonylalkyl;

R_1 represents hydrogen; an amino protecting group; or a group of formula R_5Y- wherein

R_5 represents hydrogen or an unsubstituted or substituted alkyl, alkenyl, alkinyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, heterocyclyl or heterocyclylalkyl group; and

Y represents -CO-; -NH-CO-; -NH-CS-; -SO_2-; -O-CO-; or -O-CS-;

R_2 represents arylalkyl;

R_3 represents halogen, alkyl, alkoxy or hydroxyalkoxy; and

R_4 represents 2-hydroxybenzyl which is unsubstituted or substituted in 4 position by methoxy.

4. (Withdrawn) Use of a 2,4-diamino-3-hydroxycarboxylic acid of formula I according to claim 1, wherein

A and B independently represent an amino acyl moiety, which is unsubstituted or substituted by C_1-C_4alkyl or C_1-C_4alkoxycarbonyl C_1-C_4alkyl;

R_1 represents hydrogen or a group of formula R_5Y- wherein

R_5 represents hydrogen; C_1-C_4alkyl which is unsubstituted or substituted by phenoxy, hydroxy or amino; C_2-C_4alkenyl; C_2-C_4alkinyl; C_6-C_{10}aryl; C_7-C_{12}arylalkyl which is unsubstituted or substituted by hydroxy, C_1-C_4alkyl, amino or C_1-C_4alkyl amino; pyridyl C_1-C_4alkyl; and

Y represents -O-CO- or -CO-;

R_2 represents C_7-C_{12}arylalkyl;

R_3 represents halogen, C_1-C_4alkyl, C_1-C_4alkoxy or hydroxy C_1-C_4alkoxy; and

R_4 represents 2-hydroxybenzyl which is unsubstituted or substituted in 4 position by methoxy.

5. (Withdrawn) Use of a 2,4-diamino-3-hydroxycarboxylic acid of formula I according to claim 1, wherein

A and B independently represent an amino acyl moiety, which is unsubstituted or substituted by C_1-C_4alkyl or C_1-C_4alkoxycarbonyl C_1-C_4alkyl

R_1 represents hydrogen or a group of formula R_5Y- wherein

R_5 represents hydrogen; C_1-C_4alkyl which is unsubstituted or substituted by phenoxy, hydroxy or amino; C_2-C_4alkenyl; C_2-C_4alkinyl; C_6-C_{10}aryl; C_7-C_{12}arylalkyl which is unsubstituted or substituted by hydroxy, C_1-C_4alkyl, amino or C_1-C_4alkyl amino; pyridyl C_1-C_4alkyl; and

Y represents -O-CO- or -CO-;

R_2 represents C_7-C_{12}arylalkyl;

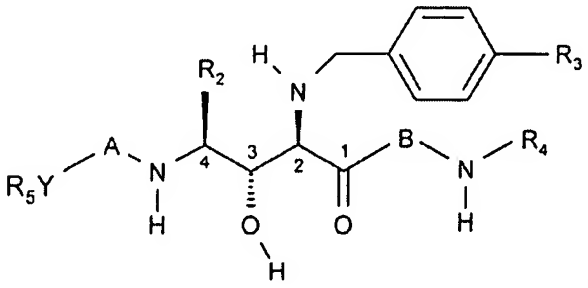
R_3 represents C_1-C_4alkoxy; and

R_4 represents 2-hydroxybenzyl substituted in 4 position by methoxy.

6. (Withdrawn) A method of treatment of warm-blooded animals, including humans, in which a therapeutically effective dose of a 2,4-diamino-3-hydroxycarboxylic acid of the formula I, in which the symbols and substituents have the meaning as given in claim 1, in free form or in pharmaceutically acceptable salt or complex form is administered to such a warm-blooded animal suffering from a proliferative disease responsive to an inhibition of the multicatalytic proteasome complex.

7. (Withdrawn) The method of claim 6 wherein the therapeutically effective dose inhibits cell proliferation in a tumor.

8. (Currently Amended) A compound of the formula I*,



(I*)

wherein

A and B independently represent an unsubstituted or substituted amino acyl moiety;

R_2 represents arylalkyl;

R_3 represents halogen, alkyl, alkoxy or hydroxyalkoxy;

R_4 represents 2-hydroxy-benzyl ~~unsubstituted or~~ substituted in 4 position by methoxy; and

R_5 represents arylalkyl and

Y represents -CO-; or

R_5 represents alkyl substituted by cycloalkyl, naphthyl, pyridyl or phenyl in which phenyl is substituted by alkyl or amino; and

Y represents -O-CO-;

or a pharmaceutically acceptable salt thereof.

9. (Previously Presented) A compound of the formula I* according to claim 8, wherein A and B independently represent L-tert.-leucine, L-valine, L-glutaminic acid methyl ester or glycine;

R_2 represents arylalkyl;

R_3 represents alkoxy;

R_4 represents 2-hydroxy-4-methoxybenzyl; and

R_5 represents arylalkyl and

Y represents -CO-; or

R_5 represents alkyl substituted by cycloalkyl, naphthyl, pyridyl or phenyl in which phenyl is substituted by alkyl or amino; and

Y represents -O-CO-;

or a pharmaceutically acceptable salt thereof.

10. (Previously Presented) A compound of the formula I* according to claim 8, wherein A and B independently represent L-tert.-leucine, L-valine, L-glutaminic acid methyl ester or glycine;

R_2 represents C_7-C_{12}arylalkyl;

R_3 represents C_1-C_4alkoxy;

R_4 represents 2-hydroxy-4-methoxybenzyl; and

R_5 represents C_7-C_{12} arylalkyl and

Y represents -CO-; or

R_5 represents C_1-C_4alkyl substituted by C_5-C_7cycloalkyl, naphthyl, pyridyl or phenyl in which phenyl is substituted by C_1-C_4alkyl or amino; and

Y represents -O-CO-;

or a pharmaceutically acceptable salt thereof.

11. (Withdrawn) A compound of formula I* according to claim 8 selected from the group of compounds consisting of

4-[4-(2-Benzyloxycarbonylamino-3-methyl-butyrylamino)-3-hydroxy-2-(4-methoxy-benzyl-amino)-5-phenyl-pentanoylamino]-4-(2-hydroxy-4-methoxy-benzylcarbamoyl)-butyric acid methyl ester;

{1-[1-Benzyl-2-hydroxy-3-[1-(2-hydroxy-4-methoxy-benzyl-carbamoyl)-2-methyl-propyl-carbamoyl]-3-(4-methoxy-benzylamino)-propylcarbamoyl]-2,2-dimethyl-propyl}-carbamic acid naphthalen-1-ylmethyl ester;

{1-[1-Benzyl-2-hydroxy-3-[1-(2-hydroxy-4-methoxy-benzylcarbamoyl)-2-methyl-propyl-carbamoyl]-3-(4-methoxy-benzylamino)-propylcarbamoyl]-2,2-dimethyl-propyl}-carbamic acid naphthalen-2-ylmethyl ester;

{1-[1-Benzyl-2-hydroxy-3-[1-(2-hydroxy-4-methoxy-benzylcarbamoyl)-2-methyl-propyl-carbamoyl]-3-(4-methoxy-benzylamino)-propylcarbamoyl]-2,2-dimethyl-propyl}-carbamic acid pyridin-4-ylmethyl ester;

{[1-Benzyl-2-hydroxy-3-[1-(2-hydroxy-4-methoxy-benzylcarbamoyl)-2-methyl-propyl-carbamoyl]-3-(4-methoxy-benzylamino)-propylcarbamoyl]-methyl}-carbamic acid benzyl ester;

{1-[1-Benzyl-2-hydroxy-3-[1-(2-hydroxy-4-methoxy-benzylcarbamoyl)-2,2-dimethyl-propyl-carbamoyl]-3-(4-methoxy-benzylamino)-propylcarbamoyl]-2,2-dimethyl-propyl}-carbamic acid benzyl ester;

and the pharmaceutically acceptable salts of these compounds.

12. (Withdrawn) A compound of formula I* according to claim 8, which is

4-[4-(2-Benzyloxycarbonylamino-3-methyl-butyrylamino)-3-hydroxy-2-(4-methoxy-benzyl-amino)-5-phenyl-pentanoylamino]-4-(2-hydroxy-4-methoxy-benzylcarbamoyl)-butyric acid methyl ester

or a pharmaceutically acceptable salt of this compound.

13. (Previously Presented) A compound of formula I* according to claim 8 selected from the group of compounds consisting of

4-[3,3-Dimethyl-2-(2-naphthalen-1-yl-acetylamino)-butyrylamino]-3-hydroxy-2-(4-methoxy-benzylamino)-5-phenyl-pentanoic acid [1-(2-hydroxy-4-methoxy-benzyl-carbamoyl)-2-methyl-propyl]-amide;

{1-[1-Benzyl-2-hydroxy-3-[1-(2-hydroxy-4-methoxy-benzylcarbamoyl)-2-methyl-propylcarbamoyl]-3-(4-methoxy-benzylamino)-propylcarbamoyl]-2,2-dimethyl-propyl}-carbamic acid 3-methylbenzyl ester;

4-{2-[3-(3-Amino-phenyl)-propionylamino]-3,3-dimethyl-butyrylamino}-3-hydroxy-2-(4-methoxy-benzylamino)-5-phenyl-pentanoic acid [1-(2-hydroxy-4-methoxy-benzylcarbamoyl)-2-methyl-propyl]-amide;

{1-[1-Benzyl-2-hydroxy-3-[1-(2-hydroxy-4-methoxy-benzylcarbamoyl)-2-methyl-propylcarbamoyl]-3-(4-methoxy-benzylamino)-propylcarbamoyl]-2,2-dimethyl-propyl}-carbamic acid 3-amino-benzyl ester;

{1-[1-Benzyl-2-hydroxy-3-[1-(2-hydroxy-4-methoxy-benzyl-carbamoyl)-2-methyl-propylcarbamoyl]-3-(4-methoxy-benzylamino)-propylcarbamoyl]-2,2-dimethyl-propyl}-carbamic acid 3,5-dimethyl-benzyl ester;

{1-[(1-Benzyl-2-hydroxy-3-[1-(2-hydroxy-4-methoxy-benzylcarbamoyl)-2-methyl-propylcarbamoyl]-3-(4-methoxy-benzylamino)-propylcarbamoyl]-2,2-dimethyl-propyl}-carbamic acid cyclohexylmethyl ester;

and the pharmaceutically acceptable salts of these compounds.

14. (Cancelled).

15. (Previously Presented) A pharmaceutical composition comprising a compound of formula I* according to claim 8 or a pharmaceutically acceptable salt of such a compound together with a pharmaceutical carrier.